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EXAMINER

[illegible]

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ART UNIT	PAPER NUMBER
1804	6

DATE MAILED: 10/15/96

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 5/18/96 ☒ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), —— ~~days~~ from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☒ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ ________________.

Part II SUMMARY OF ACTION

1. ☒ Claims 31, 33, and 34 are pending in the application.

   Of the above, claims ________ are withdrawn from consideration.

2. ☒ Claims 1-30 and 32 have been cancelled.
3. ☐ Claims ________ are allowed.
4. ☒ Claims 31, 33, and 34 are rejected.
5. ☐ Claims ________ are objected to.
6. ☐ Claims ________ are subject to restriction or election requirement.
7. ☒ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on ________. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on ________. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed ________, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. ________ ; filed on ________.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 31, 33, and 34 are rejected under 35 U.S.C. § 103 as being unpatentable over Taniguchi et al (Gene 10: 11 (1980)) in view of Roberts et al (Proc. Natl. Acad. Sci. USA 76: 5596 (1979)

and further in view of Borden (Annals of Internal Medicine 91: 472 (1979)). Taniguchi et al teaches the molecular cloning of the human IFN-ß1 gene. Roberts et al teaches the expression of a eukaryotic gene in an E. coli host cell using an expression vector. Borden suggests the use of human fibroblast interferon (i.e. ß interferon) in anti-tumor therapy. It would have been obvious to one of ordinary skill in the art at the time the invention was made to express the human IFN-ß1 gene of Taniguchi et al in the manner of Roberts et al in order to produce large amounts of human IFN-ß1 for anti-tumor therapy as suggested by Borden. This rejection is repeated for reasons already of record (e.g., Office action mailed January 16, 1996, page 4). Applicant's arguments (paper no. 5, pages 6-16 and the various attachments and exhibits alluded to therein) are not convincing. First, Applicant argues that there is no basis for the combination of Taniguchi et al and Roberts et al. Applicants urge that the claimed invention cannot have been obvious to one of ordinary skill in the art at the time the

invention was made, but applicant does not discuss the references in the manner in which they were used in the rejection. Applicant argues that there must be something to lead one of ordinary skill in the art to the reference and that there is nothing to lead one of ordinary skill in the art to Roberts et al. This conclusion is erroneous in view of the plain language used in the last paragraph of the Discussion section of Roberts et al (page 5600). It is clear that the Roberts et al approach to expression of eukaryotic genes in bacteria (E. coli) could be accomplished using the Roberts et al approach, based on the success Roberts et al reported in expressing the t antigen of SV40. Applicant does not point to any deficiency in Roberts et al in connection with gene expression, which is what Roberts et al was cited to show. Rather, applicant asserts that Roberts et al does not mention any interferon genes. The fact that Roberts et al does not mention interferon genes is not disputed and is not asserted in the rejection of the claims under 35 U.S.C. § 103. Taniguchi et al was cited to show the human IFN-ß gene.

Applicant asserts that there is nothing to suggest combining the two references. This argument cannot be persuasive since Roberts et al suggests using the expression approach they found successful for expressing SV40 t antigen for the expression of other eukaryotic genes in bacteria. Since the human IFN-ß gene is a eukaryotic gene and since Taniguchi et al cloned the human IFN-ß gene for the purpose of obtaining large amounts of interferon (e.g., see Taniguchi et al at page 11, first and second full paragraphs in the right-hand column), it is clear that one of ordinary skill in the art would have seen a connection between these two references.

Applicant cites In re Vaeck to support the notion that the claimed invention is nonobvious. The facts in the instant application differ significantly from those in Vaeck in that the Vaeck application concerned gene expression in cyanobacteria. Little was known about the expression of heterologous genes in cyanobacteria at the time of the filing of the Vaeck application. In strong contrast, the instant claims are directed to DNAs

encoding IFN-ß that are operatively linked to expression control sequences and to methods of expressing the DNA in bacterial host cells. The only examples of bacterial host cells are the well known E. coli host cells. Accordingly, the facts and issues in the instant application can be distinguished as being fundamentally different from those is Vaeck. The case of In re O'Farrell (7 USPQ2d 1673, Fed. Cir. 1988) is cited as being a better guide to the issue of obviousness in the instant application than is Vaeck. In O'Farrell, a DNA sequence encoding a nonsense polypeptide was expressed in an E. coli host cell. The Court ruled that an obviousness rejection in the expression of a foreign DNA in an E. coli host could be sustained even if there was no guarantee of success of expression of that gene. Thus, the case of O'Farrell is closer to the facts in the instant application than is Vaeck. Applicant's arguments in connection with possible roadblocks to bacterial expression of an active IFN-ß are not convincing. It is not necessary for one of ordinary skill in the art to know every detail of polypeptide

folding (indeed, such is not known even in 1994, yet many dozens of active polypeptides have been expressed in heterologous host cells) or disulfide linkage in order for the expression of a heterologous gene in bacterial host cells to be obvious. At the time the instant invention was made, the main problems confronting scientists attempting to express foreign polypeptides were the transcription of the foreign polypeptide and the translation of the mRNA produced by transcription. Both of these problems are solved in the Roberts et al publication. For example, the last paragraph of the discussion section of Roberts et al clearly indicates that the method described in that article have general use in the expression of eukaryotic genes in E. coli. Thus, the differences between t antigen expressed in the example in Roberts et al and IFN-ß are not relevant to the question of obviousness. Applicant has provided no convincing evidence that one of ordinary skill in the art would have been prevented from using the Roberts et al method in the expression

of the IFN-ß gene of Taniguchi et al simply because SV40 t antigen is not IFN-ß.

Thus, appellants have not presented convincing evidence as to why one of ordinary skill in the art would not have expressed the IFN-ß gene of Taniguchi et al in the manner taught by Roberts et al.

The copies of the declarations by Dr. Cate are not convincing. First, the declarations cite many references that were published after the effective filing date of the instant application. None of these can be given any weight because one of skill in the art would not be deterred from practicing what was outlined in the rejection by knowledge that occurred after the time at which obviousness is to be judged. The declaration executed January 30, 1995 (Exhibit F) points to four properties of the IFN-ß gene and/or protein that declarant urges would make the invention unobvious in view of the references cited (see paragraph 9, items (a)-(d) on page 3 of the declaration). First, declarant asserts that the high hydrophobicity of IFN-ß would

make the expression unobvious. Declarant cites a series of references to support the notion that IFN-ß is hydrophobic, at least one of which (Jankowski et al) was published prior to the effective filing date of the instant application. Applicant's argument merely points to the fact that fibroblast interferon is hydrophobic, but applicant does not present evidence sufficient to demonstrate that this would be enough to prevent one of ordinary skill in the art from expressing the polypeptide in bacteria. The presence of three cysteine residues is purported to present a problem in gene expression. The declarant then discusses the Mark et al Patent. None of the material in Mark et al was known as of the effective filing date of the instant application, thus the discussion of Mark et al can carry no weight in consideration of the issue at hand. Third, declarant raises the issue of codon usage and asserts that if the host organism did not have enough tRNA to read that codon, then expression would be affected. True enough, but there is no establishment of any fact that there would not have been enough

tRNA for expression of the IFN-ß gene, nor is there any evidence that one of ordinary skill in the art would have considered that to be serious enough to not express IFN-ß in bacteria. Finally, declarant asserts in the absence of any evidence (paragraph 31) that the majority of eukaryotic proteins expressed prior to 1980 did not begin with Met. This argument cannot convince of nonobviousness because no significance is connected to the alleged fact and because one may infer from the statement that some eukaryotic proteins expressed prior to 1980 did start with Met. Thus, one of ordinary skill in the art would expect yet another one (viz. IFN-ß) to be expressed as well.

Applicant's arguments (paper no. 5) in connection with the lack of glycosylation of the fibroblast interferon mentioned in the claims are not convincing. First, the Board decisions cited by applicant are not precedential. Second, the claims are not limited to methods using non-glycosylated fibroblast interferons because the host cell used to produce the interferon need be only a non-human host cell. Third, were the claims to be so limited,

Bose et al (cited here as of interest) teaches the dispensibility of the carbohydrate moiety of human fibroblast interferon in connection with the activity of human fibroblast interferon.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

Certain papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed

to Art Unit 1804 at (703) 305-3014. The faxing of such papers must conform with the rules published in the Official Gazette, 1156 OG 61 (November 16, 1993).

Any inquiry concerning this communication should be directed to J. Martinell at telephone number (703) 308-0296.

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1804.

JAMES MARTINELL, PH.D.
SENIOR LEVEL EXAMINER
GROUP 1800